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Effect of blood transfusion on octogenarians undergoing open heart surgery

Blood transfusion on octogenarians in heart surgery

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Abstract
Aim: The aim of this study was to examine the effect of perioperative allogeneic blood transfusion on early morbidity and mortality in patients aged 80 years and older undergoing cardiac surgery.
Material and Methods: Between January 2017 and December 2019, 115 patients aged eighty and over who underwent heart surgery in our institution were included in the study. The data were collected retrospectively from our hospital's records after ethical committee approval. In this study, patients were divided into two groups as those who received blood and those who did not and were compared in terms of postoperative cerebrovascular incident, new-onset dialysis, infection, prolonged ICU length of stay, and mortality.
Results: In the study, 63.5% (n=73) of the patients were female and 36.5% (n=42) were male. The CPB time of the patients who received postoperative blood transfusion was found to be statistically significantly higher. Preoperative hematocrit levels were significantly lower and postoperative morbidities and mortality rates were significantly higher in the transfusion group. Age, CPB time, postoperative dialysis, inotropic use, transfusion of more than 5 units of blood were independent factors that increases the mortality according to the univariate and multivariate analyses.
Discussion: Octogenarians are a fragile group of patients. Blood transfusion should be avoided whenever possible to minimize the risk.

Keywords
Blood Transfusion, Cardiac Surgery, Complications, Mortality, Octogenarians

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Introduction

Transfusion of allogeneic red blood cells (RBCs) has been practiced in modern medicine for many years. In some studies, it has been shown that low hemoglobin (Hb) concentrations and the resulting decreased oxygen delivery increase mortality [1]. Patients with low hematocrit at the time of coronary artery bypass graft (CABG) surgery had higher mortality [2]. However, transfusion also has some handicaps. There is a growing debate that transfusion of RBCs during the treatment of cardiac surgery patients increases short and long-term morbidity and mortality. In addition to mortality, it has been stated that transfusion in critically ill patients carries high morbidity rates [3].

In a number of studies, it has been associated with many morbidities, including increased renal failure and infection, as well as respiratory, cardiac and neurological complications [4-5]. The rate of allogeneic blood transfusion in patients undergoing cardiac surgery varies between 40% and 90%, although it varies in many centers [6,7]. Today, as a result of technological developments and new treatment options, the average life expectancy has increased gradually. For this reason, the proportion of octogenarians among patients undergoing cardiac surgery is increasing. Due to the high incidence of age-related anemia in octogenarians, the probability of transfusion is higher [8]. However, the effects of blood transfusion in octogenarians undergoing cardiac surgery have not been clearly demonstrated. In most studies, patients in heterogeneous age groups were compared [1,3,5,9]. In our study, we selected a group of patients in the homogeneous age group and examined only patients aged eighty years and older. The aim of this study was to examine the effect of perioperative allogeneic blood transfusion on early morbidity and mortality in patients aged 80 years and older undergoing cardiac surgery.

Material and Methods

This study was conducted based on the linked data collected retrospectively from our hospital's records after approval by the hospital ethics committee (E-28001928-604.01.01). The study included 115 patients (n=115) aged 80 years and older who underwent cardiac surgery in our institution between January 2017 and December 2019. All emergency and elective cases were included in the study. Patients were operated on pump and were monitored with 20 G radial artery catheterization, 5-lead electrocardiography (ECG), peripheral oxygen saturation (sPO2) and Bispectral index (BIS) after 16 G peripheral IV catheter was inserted. Anesthesia induction was achieved with propofol, fentanyl and rocuronium by applying the routine cardiopulmonary bypass (CPB) anesthesia protocol. Propofol, Fentanyl, Rocuronium and Sevoflurane were used for maintenance anesthesia. Patients were started with 1 g bolus tranexamic acid followed by intravenous infusion of 7.5 mg/kg/hour. A transesophageal echocardiography probe was placed in all patients to evaluate perioperative cardiac functions. According to the transfusion protocol of our hospital, RBC were transfused in a way that hemoglobin was 7-8 g/dl (Htc 21-24) during CPB and 9-10 g/dl (Htc 27-30) after CPB. Operations were performed with sternotomy. Before cannulation, 300-400 IU/kg heparin was administered. Arterial cannulation was performed using the ascending aorta. Venous cannulation was performed with bicaval (in patients who will undergo mitral or tricuspid valve intervention) or two-stage single atrial venous cannula technique. CPB was initiated with activated coagulation time (ACT) >450. All operations were performed at 32 degrees hypothermia, under cross clamp and on pump. Isothermic blood cardioplegia at 20-minute intervals was used for myocardial protection.

After termination from CPB, the ratio of heparin to protamine was neutralized to 1:1. At the end of the operation, the patients were taken to the postoperative intensive care unit (ICU).

In this study, patients were divided into two groups as those who received blood and those who did not, and were compared in terms of postoperative cerebrovascular incident (CVI), new-onset dialysis, infection, prolonged ICU length of stay, and mortality.

The definition of postoperative CVI is used for temporary or permanent neurologic deficits. The definition of postoperative dialysis was used for patients with normal preoperative renal function who were started on dialysis for postoperative acute renal failure (ARF). The definition of postoperative infection was used for patients with a positive wound or blood culture and who were initiated on antibiotic therapy. The definition of prolonged intensive care unit stay was used for patients who stayed in the intensive care unit for more than 48 hours. The definition of mortality was used for patients who died in the early period in the hospital.

Statistical Analysis

SPSS v26.0 program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used while evaluating the study data. The conformity of the quantitative data to the normal distribution was tested with the Shapiro-Wilk test and graphical examinations. Student's t-test was used for comparisons between two groups of normally distributed quantitative variables, and the Mann-Whitney U test was used for comparisons between two groups of non-normally distributed quantitative variables. The Chi-square test, Fisher's exact test, and Fisher-Freeman-Halton test were used to compare qualitative data.

Univariate and Multivariate Logistic regression analyzes were used to evaluate the risk factors affecting mortality. Statistical significance was accepted as p<0.05.

Results

The study was conducted in S.B.U. Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital between January 2017 and December 2019 with a total of 115 cases, 63.5% (n=73) were females and 36.5% (n=42) were males. The ages of the subjects participating in the study ranged from 80 to 97 years, with an average of 82.90±3.09 years. Age and gender distributions and BMI measurements of the cases did not show a statistically significant difference according to the status of postoperative blood transfusion (p>0.05). The rate of diabetic patients and the rate of hypertension in patients who received postoperative blood transfusion were found to be statistically significantly higher than the patients who were not transfused (respectively p=0.007, p=0.039; p<0.05). There was no statistically significant difference between the distribution of the operation types of the cases according to the status of postoperative blood transfusion (p>0.05) (Table 1).

Preoperative and postoperative EF and Cross-Clamp Time measurements of the cases did not show a statistically significant difference according to the status of postoperative blood transfusion (p>0.05). The CPB time of the patients who received postoperative blood transfusion was found to be statistically significantly higher than the patients who did not (p=0.043; p<0.05). There was no statistically significant difference between the preoperative lowest hematocrit (HCT), creatinine measurements of the cases according to the status of postoperative blood transfusion (p>0.05). The preoperative HCT value of the patients who received postoperative blood transfusion was found to be statistically significantly lower than in the patients who did not (p=0.017; p<0.05) (Table 1).

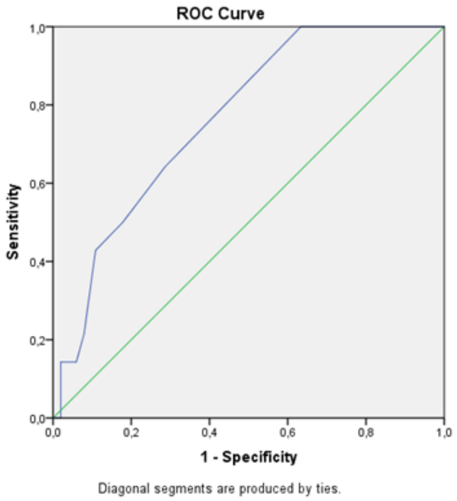

Figure 1. Diagnostic Screening Tests and ROC Curve Results for Blood Unit Count

No statistically significant difference was found between the incidence of postoperative CVI in the cases according to the status of postoperative blood transfusion (p>0.05). The incidence of postoperative dialysis in patients who received postoperative blood transfusion was found to be statistically significantly higher than in patients who were not transfused (p=0.029; p<0.05). The incidence of postoperative infection in patients who received postoperative blood transfusion was found to be statistically significantly higher than in patients

Table 1. Evaluation of descriptive characteristics according to postoperative blood transfusion status

		Total	Postoperative Blood Transfusion		p-value
			(-)	(+)	
Age	Min-Max (Median)	80-97 (82)	80-89 (82)	80-97 (83)	[a]0,317
	Mean±SD	82,90±3,09	82,34±2,33	83,17±3,39	
Gender	Female	73 (63,5)	28 (73,3)	45 (58,4)	[b]0,110
	Male	42 (36,5)	10 (26,3)	32 (41,6)	
BMI	Min-Max (Median)	15,5-37 (27,6)	19-36,7 (27,9)	15,5-37 (27,3)	[c]0,903
	Mean±SD	27,76±4,51	27,68±4,41	27,79±4,58	
DM	(-)	61 (53,0)	27 (71,1)	34 (44,2)	[b]0,007**
	(+)	54 (47,0)	11 (28,9)	43 (55,8)	
Hypertension	(-)	63 (54,8)	26 (68,4)	37 (48,1)	[b]0,039*
	(+)	52 (45,2)	12 (31,6)	40 (51,9)	
Operation	Elective	88 (76,5)	32 (84,2)	56 (72,7)	[b]0,172
	Emergent	27 (23,5)	6 (15,8)	21 (27,3)	
Operation type	CABG	66 (57,4)	26 (68,4)	40 (51,9)	[d]0,091
	Valve surgery	18 (15,7)	7 (18,4)	11 (14,3)	
	AVR+CABG	16 (13,9)	4 (10,5)	12 (15,6)	
	MVR+CABG	5 (4,3)	0 (0,0)	5 (6,5)	
	Aortic surgery	8 (7,0)	0 (0,0)	8 (10,4)	
	Other	2 (1,7)	1 (2,6)	1 (1,3)	
Preoperative EF	Min-Max (Median)	25-65 (55)	25-60 (55)	25-65 (55)	[a]0,983
	Mean ± SD	51,53±9,52	51,84±8,81	51,38±9,9	
Postoperative EF	Min-Max (Median)	25-60 (50)	25-60 (50)	25-60 (50)	[a]0,204
	Mean±SD	47,35±9,81	49,61±7,92	46,23±10,49	
CPB	Min-Max (Median)	43-207 (113)	43-207 (100,5)	45-200 (125)	[c]0,043*
	Mean±SD	118,87±37,1	108,92±39,91	123,78±34,86	
Cross-clamp time	Min-Max (Median)	25-831 (85)	25-701 (75)	25-831 (88)	[a]0,117
	Mean±SD	102,41±96,21	98,89±107,66	104,14±90,73	
Preoperative lowest HCT	Min-Max (Median)	14,7-66 (25,3)	19,3-33,2 (25,8)	14,7-66 (25,2)	[a]0,938
	Mean ± SD	25,66±5,48	25,52±3,59	25,73±6,23	
Preoperative Creatinine	Min-Max (Median)	0,6-5,8 (0,95)	0,7-1,5 (0,99)	0,6-5,8 (0,95)	[a]0,866
	Mean±SD	1,09±0,55	1,02±0,23	1,13±0,66	
Preoperative HCT	Min-Max (Median)	18,9-50,5 (35,6)	28,8-50,5 (36,2)	18,9-49,8 (35)	[c]0,017*
	Mean±SD	35,7±5,94	37,58±5,87	34,78±5,79	

[a]Mann-Whitney U Test; [c]Student-t Test; *p<0,05. [a]Mann Whitney U Test, [b]Pearson's Chi-Square Test, [c]Student-t Test, [d]Fisher-Freeman-Halton Test AVR: aortic valve replacement, BMI: Body mass index, CABG: coronary artery bypass grafting, DM: Diabetes Mellitus, MVR: mitral valve replacement. *p<0,05, **p<0,01. CPB: cardiopulmonary bypass, EF: ejection fraction, HCT: hematocrit

who were not transfused (p=0.031; p<0.05).

The incidence of postoperative IABP in patients who received postoperative blood transfusion was found to be statistically significantly higher than in patients who were not transfused (p=0.029; p<0.05). The rate of prolonged intensive care hospitalization and the rate of use of inotropes in patients who received postoperative blood transfusion was found to be statistically significantly higher than in patients who were not transfused (p=0.001; p<0.01).

The incidence of morbidity in patients who received postoperative blood transfusion was found to be statistically significantly higher than in patients who were not transfused (p=0.001; p<0.01). Mortality rate in patients who received postoperative blood transfusion was found to be statistically significantly higher than in patients who were not transfused (p=0.033; p<0.05) (Table 2).

Table 2. Comparisons by postoperative blood transfusion status

		Postoperative Blood Transfusion			Total
		Total n (%)	(-) n (%)	(+) n (%)	
Postoperative CVI	(-)	108 (93,9)	38 (100,0)	70 (90,9)	^{e}0,094
	(+)	7 (6,1)	0 (0,0)	7 (9,1)	
Postoperative Dialysis	(-)	105 (91,3)	38 (100,0)	67 (86,8)	^{b}0,029*
	(+)	10 (8,7)	0 (0,0)	10 (13,2)	
Postoperative Infection	(-)	97 (84,3)	36 (94,7)	61 (79,2)	^{b}0,031*
	(+)	18 (15,7)	2 (5,3)	16 (20,8)	
Postoperative IABP	(-)	106 (92,2)	38 (100,0)	68 (88,3)	^{e}0,029*
	(+)	9 (7,8)	0 (0,0)	9 (11,7)	
Prolonged ICU Stay	(-)	81 (70,4)	37 (97,4)	44 (57,1)	^{b}0,001**
	(+)	34 (29,6)	1 (2,6)	33 (42,9)	
Inotrope Use	(-)	78 (67,8)	35 (92,1)	43 (55,8)	^{b}0,001**
	(+)	37 (32,2)	3 (7,9)	34 (44,2)	
Morbidity	(-)	71 (61,7)	32 (84,2)	39 (50,6)	^{b}0,001**
	(+)	44 (38,3)	6 (15,8)	38 (49,4)	
Mortality	(-)	101 (87,8)	37 (97,4)	64 (83,1)	^{b}0,033*
	(+)	14 (12,2)	1 (2,6)	13 (16,9)	

^{b}Pearson's Chi-Square Test; ^{e}Fisher's Exact Test; *p<0,05; **p<0,01. CVI: cerebrovascular incident, IABP: intra-aortic balloon pump, ICU: intensive care unit

Table 3. Univariate and multivariate evaluation results with logistic regression analysis of factors affecting mortality

		Univariable		Multivariable	
		ODDS (%95 CI)	p	ODDS (%95 CI)	p
Age		1,24 (1,06- 1,46)	^{a}0,007*		
Gender	Female	2,62 (0,84-8,14)	^{b}0,096		
DM		2,24 (0,70-7,16)	^{b}0,174		
Hypertension		2,42 (0,76-7,76)	^{b}0,135		
Emergency surgery		3,8 (1,20-12,0)	^{b}0,023*	3,58 (0,88-14,49)	0,074
Preoperative EF		0,99 (0,93-1,05)	^{a}0,859		
Postoperative EF		0,95 (0,91-0,99)	^{a}0,035*		
CPB		1,02 (1,00-1,04)	^{c}0,004*	1,02 (0,99-1,404)	0,066
Cross clamp time		1,004 (1,00-1,01)	^{a}0,058		
Preoperative HCT		0,94 (0,85-1,04)	^{a}0,207		
Postoperative CVI		3,13 (0,54-17,9)	^{e}0,400		
Postoperative Dialysis		6,27 (1,51-26,01)	^{e}0,011*		
Postoperative Infection		2,70 (0,63-11,48)	^{b}0,180		
Blood unit >5		6,14 (1,79-20,99)	^{e}0,004*	5,24 (1,33-20,68)	0,018*
Inotrope Use		6,85 (1,98-23,69)	^{b}0,002*		

CPB: cardiopulmonary bypass, CVI: cerebrovascular incident, DM: diabetes mellitus, EF: ejection fraction, HCT: hematocrit; *p<0,05

In the ROC analysis with total blood unit counts according to mortality, a the area under curve was 0.764 (95% Confidence Interval 0.651- 0877; P=0.01). When the total blood unit cut off value was accepted as ≥ 3, sensitivity was 64.3%, specificity was 71.3% When the total blood unit cut off value was accepted as ≥ 5, sensitivity was 42.9%, specificity was 89.2% (Figure 1). The rate of emergency surgery was found to be significantly higher in patients with mortality (p=0.023; p<0.05). The ODDS ratio of the effect of emergency surgery on mortality increases by 3.8 times (1.20-12.0). While preoperative EF measurements of the cases did not differ statistically according to mortality (p>0.05), postoperative EF was found to be significantly lower in patients with mortality (p=0.035; p<0.05). The ODDS ratio of the effect of one unit increase in postoperative EF on mortality was 0.95 (0.91-0.99)

In terms of mortality, the duration of CPB was found to be significantly higher (p=0.004, p<0.05). The ODDS ratio of the effect of each unit increase in the duration of CPB on mortality increases by 1.02 (1.00-1.04) times. Postoperative dialysis rate in cases with mortality was found to be statistically significantly higher than in cases without mortality (p=0.011; p<0.05). The effect of undergoing postoperative dialysis on mortality increases the ODDS rate by 6.27 (1.51-26.01) times. Postoperative blood transfusion rate of 5 units or more in patients with mortality was found to be statistically significantly higher than in patients without mortality (p=0.004; p<0.01). The effect of having 5 or more blood units used in the cases on mortality increased the ODDS ratio by 6.14 (1.79-20.99) times. The rate of use of inotropes in cases with mortality was found to be statistically significantly higher than in cases without mortality (p=0.002; p<0.01). The ODDS ratio of the inotropic use on mortality was found to be 6.85 (1.98-23.69) in the cases. In the multivariable evaluation, emergency operation, duration of CPB and use of more than 5 units of blood were found to be the risk factors, which have a significant impact on mortality, and logistic regression analysis was performed. It was observed that the number of transfused blood units of 5 and above was statistically significant in the multivariate analysis upon mortality (p:0.018; p<0.05). The ODDS ratio of the effect of the number of transfused blood units on mortality was found to be 5.24 (1.33-20.68) (Table 3).

Discussion

Transfusion is a cause of morbidity and mortality for all age groups. It has been shown that comorbidities increase regardless of age in patients undergoing RBC transfusion [10]. Elderly patients may need more transfusions than younger patients, which increases the risk further. Our study also showed that the mortality and morbidity rates are increased with blood transfusions. We should avoid transfusion whenever possible. In today's world with all the developments and new methods, elderly patients can also be operated safely. It is now accepted that cardiac surgery can also be safely performed in the octogenarians [11]. However, we also know that advanced age is a preoperative risk factor for mortality. One of the most commonly used risk stratification method is Euro SCORE II. Age is the main risk factor that should be considered [12]. Therefore, the mortality rate of this group is slightly higher than that of the younger populations. A study by Chan et al. showed that the overall mortality in cardiac surgery in 11190 patients is 2.2% [13]. However, mortality can be up to 15% in patients over 80 years of age [14]. In our study, the mortality rate was slightly lower (12.2%).

Cardiac surgery is one of the most common surgeries involving blood transfusion. It is riskier than many surgeries in terms of morbidity and mortality. Increasing transfusion rates are one of the main reasons for this situation. For this reason, many clinics and associations continue to seek ways to reduce blood use today. Even with a restricted approach, 11.4% of the patients receive blood products [15]. In a study by Shaw et al. it is showed that not only operative mortality, but 5-year mortality was also increased by blood transfusion [16]. Similar to the literature, our study showed that blood transfusion significantly increases the mortality and morbidity of the patients.

As we discussed earlier, octogenarians are a fragile group. Already the operative mortalities are higher in this group. Our results showed that, as the amount of blood used increases, its effect on mortality increases up to 6 times. Only one patient died in the group without the blood transfusion. There are 13 patients with mortality in the transfusion group. Thus, it is safe to say that blood transfusion itself is a predictor of mortality. Blood transfusion causes morbidity as well as mortality. Increased blood product use causes increased intubation time, prolonged ICU stay, and prolonged hospital stay [17]. Similarly, in our study, the transfusion group had prolonged ICU stay.

Acute kidney injury (AKI) following cardiac surgery is one of the greatest complications. Blood transfusion itself is also an underlying cause of AKI. Numerous observational studies showed the correlation between these two factors [18]. In a study by Rasmussen et al. they detected acute renal failure in 542 of 1960 patients. In our study, we find that postoperative need for dialysis is significantly higher in patients with blood transfusion.

In light of all this information we have, the more we reduce the blood transfusion, the lower the mortality and morbidity. It is seen that blood transfusion increases mortality both with the inflammation it creates and the morbidities it creates. Although octogenarians can be operated safely today, they are still a risk group in terms of mortality. Adding an additional transfusion burden to this patient group increases the existing risks.

Therefore, transfusion should be avoided as much as possible in every patient group, but especially in octogenarians.

Conclusion

Octogenarians are a fragile group of patients. Cardiac surgery can be safely performed on these patients. However, blood transfusion should be avoided whenever possible to minimize the risk.

Limitations

Our study has some limitations. It is important to increase the number of patients with larger, multicenter series. The exact causes of mortality and morbidity can be revealed more clearly by considering risk factors one by one in larger series.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards

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Conflict of interest

The authors we have no conflict of interest to declare.

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